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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,353	04/11/2002	Edward S. Yeung	215390	6921

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EXAMINER	
STOCK JR, GORDON J	
ART UNIT	**PAPER NUMBER**
2877	

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,353	YEUNG ET AL.	
	Examiner	Art Unit	
	Gordon J Stock	2877	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 57-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-23,57-65 and 67-91* is/are rejected.

7)☒ Claim(s) *2 and 66* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *20020909* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. **Claims 7 and 71** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. The term "small molecule" in **claims 7 and 71** is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In addition, a molecule is small by definition; therefore, the size of the molecule is rendered indefinite.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. **Claims 1, 3-8, 11-13, 15-18, 21, 22, 58, 60-62, 65, 67-72, 74-76, 78-80, 83, 84, 86, 88 and 89** are rejected under 35 U.S.C. 102(e) as being anticipated by **Simpson et al. (6,485,625)**.

As to **claims 1, 3-8, 11-13, 15-18, 21, 22, 58, 60-62** Simpson discloses the following: subjecting a sample comprising multiple molecules, at least one molecule is labeled to electrophoresis; imaging the mobility of each labeled molecule over time by detecting the position of the label over time; dispersing the imaging by a transmission grating; determining the electrophoretic mobility and the molecular spectrum; distinguishing at least one molecule; at least one molecule is a nucleic acid and/or protein detectably labeled with a fluorescent dye; said sample comprises a buffer; the at least one molecule with label has fluorescence induced by a laser; the fluorescence is focused on the imaging means; using an intensified CCD camera, TE/CCD 1023E detector from Princeton Instruments Inc.; laser filters are positioned in front of said imaging means; multiframe method is used; the mobility is imaged in less than about 5 milliseconds, 4000 frames per .1 second; at least one molecule is at a concentration of at least about 1 copy per milliliter, .5 microliters of sample was analyzed was loaded into the gel. The system comprising: an electrophoretic sample channel; a monochromatic light source that irradiates sample; imaging means; a transmission grating; a lens between said light source and sample for focusing light; imaging means is an intensified CCD camera, TE/CCD 1023E detector; at least one filter, a laser filter; imaging means images 4000 frames per .1 second (Figs. 1, 2a, 2b, 3, 11-13, 14a, 14b, 17(1), 17(2), 18a, 18b; col. 5, lines 20-30 and 50-67; col. 6, lines 1-15 and 45-55; col. 7, lines 5-20 and 60-67; col. 8, lines 1-30; col. 9, lines 60-65; col. 10, lines 20-65; cols. 11-12; cols. 31-32; col. 40, lines 15-55).

As to **claims 65, 67-72, 74-76, 78-80, 83, 84, 86, 88 and 89,** Simpson discloses the following: introducing a sample comprising multiple molecules in free solution at least one is detectably labeled into a sample channel; imaging the position of labeled molecule and

dispersing image by a transmission grating; determining molecular spectrum; distinguishing at least one molecule; the molecule may be a labeled nucleic acid or protein; sample comprises a buffer; the labeled sample is fluoresced by a laser; there is focusing of the fluorescent label on imaging means; an intensified CCD camera, TE/CCD 1023E detector, comprises the imaging means; a laser filter is positioned before the imaging means; imaging happens in 4000 frames per .1 second; .5 microliters of sample is analyze. The system itself comprises the following: a sample channel; a light source of one wavelength that irradiates labeled molecules; imaging means; transmission grating; a lens between light source and channel for focusing; a TE/CCD 1023E detector; a laser filter; imaging means images 4000 frames per .1 second. (Figs. 1, 2a, 2b, 3, 11-13, 14a, 14b, 17(1), 17(2), 18a, 18b; col. 5, lines 20-30 and 50-67; col. 6, lines 1-15 and 45-55; col. 7, lines 5-20 and 60-67; col. 8, lines 1-30; col. 9, lines 60-65; col.10, lines 20-65; cols. 11-12; cols. 31-32; col. 40, lines 15-55).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. **Claims 9, 10, 73,** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in view of **Schwartz et al. (6,221,592) and Chu (5,215,883).**

As to **claims 9, 10, 73**, Simpson discloses everything as above (see **claims 8 and 72**). He is silent concerning photobleaching. However, Schwartz in nucleic acid sequencing teaches photobleaching for eliminating fluorescence signals between cycles and to eliminate bulky

moieties after they have served their purpose (col. 33, lines 55-67). In addition, Chu in electrophoretic system teaches photobleaching for demarcation of areas for detection (col. 8, lines 10-50). Therefore, it would be obvious to one skilled in the art to photobleach the buffer in order to eliminate possible fluorescent signals after certain substituents have served their purpose and/or possibly to demarcate areas for detection. Simpson does disclose a sieving matrix (col. 19, lines 60-67).

8. **Claims 14, 23, 57, 77, 85** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in view of **Yguerabide et al. (6,586,193)** and **Hayashizaki et al. (6,120,667).**

As to **claims 14, 23, 57, 77, 85**, Simpson discloses everything as above (see **claims 12, 21, 22, 75, 84** above). He is silent concerning a pinhole and equilateral prism. Yguerabide teaches in an analyte assay using labels that equilateral prisms are used to enhance to signal to noise (col. 59, lines 20-45). Therefore, it would be obvious to one skilled in the art to have the system comprise an equilateral prism to enhance signal to noise of the system. Hayashizaki in an electrophoresis apparatus teaches a pinhole to limit the detection field (col. 7, lines 15-25). Therefore, it would be obvious to one skilled in the art to have the system comprise a pinhole in order to limit the detection field.

9. **Claims 19, 20, 63, 64, 81, 82, 90, 91** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)**

As to **claims 19, 20, 63, 64, 81, 82, 90, and 91,** see **claims 1, 21, 65, and 83** above. As for the acquisition rates Simpson is silent. However, the acquisition rate depends on several factors such as electrode voltage, electrophoretic mobility, frame rate, image processing rate, and

fluorescence. This acquisition rate would be considered an optimized value. Simpson discloses the claimed invention except for the particular acquisition rates. It would have been obvious to one having ordinary skill in the art at the time of the invention was made to have the particular acquisition rates, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980)

10. **Claims 59 and 87** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Simpson et al. (6,485,625)** in evidence of **Brumley et al. (5,538,613)**.

As for **claims 59 and 87**, Simpson discloses everything as above (see **claims 58 and 86**). In addition, Simpson discloses objective lenses (col. 12, lines 1-40). In addition, Brumley in an electrophoresis analyzer teaches using a microscope objective for focusing (Fig. 1). Therefore, it would be obvious to one skilled in the art at the time the invention was made to have the system comprise a microscope objective lens to focus light to the imaging means.

Allowable Subject Matter

11. **Claims 2 and 66** are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

As to **claims 2 and 66**, the prior art of record, taken alone or in combination, fails to disclose or render obvious in a high-throughput method of distinguishing at least one molecule individually not amplifying the sample prior to being introduced into channel and/or subjected to electrophoresis, in combination with the rest of the limitations of **claims 2 and 66.**

Conclusion

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

United States Patent Application Publication 2003/0223059 to Li

U.S. Patent 6,233,048 to Parce

U.S. Patent 5,948,231 to Fuchs et al.

U.S. Patent 5,932,080 to Likuski

U.S. Patent 5,810,985 to Bao et al.

Fax/Telephone Numbers

If the applicant wishes to send a fax dealing with either a proposed amendment or a discussion with a phone interview, then the fax should:

1) Contain either a statement "DRAFT" or "PROPOSED AMENDMENT" on the fax cover sheet; and

2) Should be unsigned by the attorney or agent.

This will ensure that it will not be entered into the case and will be forwarded to the examiner as quickly as possible.

Papers related to the application may be submitted to Group 2800 by Fax transmission. Papers should be faxed to Group 2800 via the PTO Fax machine located in Crystal Plaza 4. The form of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CP4 Fax Machine number is: **(703) 872-9306**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gordon J. Stock whose telephone number is (703) 305-4787.
The examiner can normally be reached on Monday-Friday, 10:00 a.m. - 6:30 p.m.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0956.

gs
December 14, 2003

Zandra V. Smith
Primary Examiner
Art Unit 2877